UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/673,794	12/20/2000	Ilkka Larma	06267.0053	4230

7590 09/24/2002

Finnegan Henderson Farabow Garrett & Dunner
1300 I Street N W
Washington, DC 20005

EXAMINER	
JOYNES, ROBERT M	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 09/24/2002 13

Please find below and/or attached an Office communication concerning this application or proceeding.

1-4, 11, 15, 16

5-10, 12-14, 17

Office Action Summary	Application No. 09/673,794	Appli ant(s) LARMA ET AL.	
	Examiner Robert M. Joynes	Art Unit 1615	

-- Th MAILING DATE of this communication appears on the cover sheet with th correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt is acknowledged of applicants' Preliminary Amendment filed on October 20, 2000.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 recites that the active agent is to be release *substantially completely* before the active agent reaches the large intestines. It is unclear what applicants are trying to convey by the phrase s*ubstantially completely.*

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6 and 8-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frisbee et al. (US 5213811) in view of Haikala et al. (WO 9321921) or Haikala in view of Frisbee.

Frisbee teaches a sustained release drug composition comprising two different release profile compositions (Col. 1, line 61 – Col. 2, line 62). One component is a sustained release composition (Col. 2, lines 19-21) and the second is a rapid release (Col. 2, lines 27-30). The sustained release component comprises a bead on which a coating of the drug, hydroxypropyl methylycellulose and a plasticizer (Col. 1, line 61 – Col. 2, line 21). This component is further coated with a mixture of ethyl cellulose, hydroxypropyl cellulose, polyvinyl acetate phthalate and a plasticizer (Col. 2, lines 8-18). The rapid release component has the same coatings as the sustained release component but has an additional coating of the drug layer on the outside of the bead or as an end layer (Col. 2, lines 22-26). The active agent of the composition is milrinone (Col. 3, lines 9-21).

Frisbee does not expressly teach that the active agent is levosimendan or the exact concentration ranges of the specific components.

Haikala teaches the drug levosimendan as a known an anti-ischemic drug (Page 1, lines 1-29). The drug is a known PDE III inhibitor along with pimobendan and milrinone (Page 1, lines 21-23). These compounds can be formulated into tablets, dragees, capsules, suppositories, emulsions, suspensions or solutions with suitable

carriers, solvents, gel forming ingredients, dispersion forming ingredients, antioxidants, colors, sweeteners and wetting agents (Page 1, line 30 – Page 2, line 13).

While the reference does not teach the complete concentration range, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to combine the teaching of Frisbee with the teachings of Haikala. Frisbee teaches a formulation of milrinone wherein two release profiles are achieved with release controlling substances. Haikala teaches that levosimendan is a known PDE III inhibitor like milrinone. It would be obvious to substitute on known PDE III inhibitor for another known inhibitor.

One of ordinary skill in the art would have been motivated to do this to achieve a similar result with a similar active agent. One would be motivated by availability of the active agents. One would also be motivated to prepare formulations of similar active to suit the desired host.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to combined the teachings of Haikala with those of Frisbee.

Haikala teaches a known anti-ischemic drug and other similar drugs. Haikala further teaches that various formulations with known pharmaceutical substances can be made by one of ordinary skill in the art. Frisbee teaches one such formulation with a known anti-ischemic drug wherein two release profiles are achieved.

One of ordinary skill in the art would have been motivated to do this to prepare levosimendan in a sustained release formulation. Again, one would be motivated by the availability of the active agent and by the effectiveness for the desired host.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Frisbee in view of Haikala further in view of Yarwood et al. (EP 0091767) or Haikala in view of Frisbee further in view of Yarwood et al. The teachings of Frisbee and Haikala are discussed above. Neither Frisbee nor Haikala teach the addition of microcrystalline cellulose as an excipient.

Yarwood teaches that microcrystalline cellulose is a known excipients to be used in pharmaceutical formulations.

Whether Yarwood is taken with Frisbee in view of Haikala or Haikala in view of Frisbee, at the time the invention was made, it would have been obvious to a person of ordinary skill in the art to include known excipients such as microcrystalline cellulose in the formulation including levosimendan. Haikala teaches that any suitable components may be included in formulations of levosimendan. Microcrystalline cellulose is a known pharmaceutical component.

One of ordinary skill in the art would have been motivated to do this to add weight to the formulation or add filler to a capsule or tablet.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M. Joynes whose telephone number is (703) 308-8869. The examiner can normally be reached on Monday through Friday 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (703) 308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Robert M. Joynes
Patent Examiner
Art Unit 1615
September 19, 2002

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600